AMENDMENTS

Amendments to the Specification:

Please replace the paragraph beginning at page 24, line 15, which with the following amended paragraph:

In one particular embodiment of the present invention, peptides are used as agents to interfere with the eIF-4E-4E-BP1 interaction or to interfere with desequestration of eIF-4E. In one particular embodiment, a peptide capable of sequestering eIF-4E contains at least 7 amino acids, and preferably between at least 14 and 16 amino acids with at least 80% sequence identity to the amino acid sequences of the 4E-BPs shown below or of the 4E-binding sites also shown hereinbelow. In one particular embodiment of the present invention, the sequestering peptide comprises a consensus sequence selected from: YxxxxLϕ (SEQ ID NO: 21), +ϕxxYx+xf$\phi\phi$ (SEQ ID NO: 22), +$\phi\phi$Y-+xF/A$\phi\phi$xxRxSP (SEQ ID NO: 23), and +$\phi\phi$Y-+xfLϕxxRxSP (SEQ ID NO: 24). Preferably, the sequestering peptide having the ability to bind to eIF-4E and thereby modulate energy homeostasis in an animal contains between 7 and 16 amino acids with at least 95% sequence identity to the amino acid sequence of the 4E-binding sites shown in the figures below. More preferably, the sequestering peptide has a 100% sequence identity to the amino acid sequences shown in the figures and even more preferably, 100% sequence identity with mammalian 4E-binding sites and particularly human rat mouse 4E-binding sites. Conversely, it shall be understood that eIF-4E desequestering agents can in certain embodiments be selected from peptides which bind to 4E-BPs. In one particular embodiment, such peptides are selected from 4E-BP interaction domain of eIF-4E.

Please replace the paragraph beginning at page 43, line 27, with the following amended paragraph:

As seen in Figures 6 and 7, the eIF4E binding sites (or eIF4E interaction domains) of numerous protein from evolutionarily distant organisms show a significant homology/identity. In addition, the sequences of rat and mouse 4E-BP1, 4E-BP2 and 4E-BP3 are 100% identical to those of the human in the region presented here. Indeed, consensus sequences which retain their eIF4E binding activity are provided. For example, a consensus 4E-binding sites of 4E-BPs is +ϕϕY-+xF/Aϕϕxx RxSP (SEQ ID NO: 23) wherein + and - refer to a charged amino acid; ϕ is a hydrophobic amino acid; x is any amino acid; and the capital letters refer to the known one letter code for amino acids. Preferably, the consensus sequence has the sequence ~~+ ϕϕY -+xfLϕxxRxSP~~ +ϕϕY-+xfLϕxxRxSP (SEQ ID NO: 24), wherein f refers to a preferred but apparently the non-essential amino acid Phe (the rest is as for the previous consensus sequence). In yet another embodiment, the 4E-binding consensus sequence has the sequence +ϕxxYx+Xfϕϕ (SEQ ID NO: 22) or YxxxxLϕ (SEQ ID NO: 21). Conversely, they could be used to design eIF-4E or negative regulators thereof, which no longer interact or show lower affinities. These consensus sequences could be used as eIF4E sequestering agents or as starting points to design other eIF4E sequestering agents.

Please replace the paragraph beginning at page 45, line 8, with the following amended paragraph:

4E-BP1 expression vector was constructed as follows: the mouse 4E-BP1 cDNA was cloned by RT-PCR using sense primer 5'- TGCAGGAGACATGTCG-3' (SEQ ID NO: 1) and anti- sense primer 5'-ACAGTTTGAGATGGAC-3' (SEQ ID NO: 2), with SUPERSCRIPTII™ (GIBCO-BRL) and Pfu polymerase (TOYOBO). It was sequenced and subcloned under the control of a CAG promoter (AG promoter with CMV-IE enhancer). A puromycin resistant cassette was derived from the pBabe-PURO vector and introduced into the 4E-BP1 expression vector, which was transfected (4 mg) into MEF cells (6 cm dishes) with Lipofectin (Gibco-BRL). T7-CAT was described previously and EMCV CAT was kindly provided by Dr. Sung-Key Jang (POHANG Institute of Science and Technology, Korea).

Please replace the paragraph beginning at page 46, line 3, with the following amended paragraph:

MEF cells were transfected with T7-CAT and T7-EMCV-CAT plasmids by Lipofectin, followed by infection with a recombinant vaccinia virus expressing the T7 RNA polymerase gene (LOT7-1 RVV) as described previously (Takeuchi et al., 1999). RNA quantitation was performed by a real time detection PCR method using a sense primer (5'-GGGTGAGTTTCACCAGTTTTGA-3'; SEQ ID NO: 3), an anti-sense primer (5'-CCACTCATCGCAGTACTGTTGT-3'; SEQ ID NO: 4), and a probe (5'(FAM)-CAATATGGACAACTTCTTCGCCCC-(TAMRA)3'; SEQ ID NO: 5), as described previously (Yasui et al.,1998). Expressed CAT protein was measured by CAT-ELISA (Roche).